

VANDERBILT MEMORY & ALZHEIMER'S CENTER

Background

- Enlarged perivascular spaces (ePVS) are a key marker of cerebral small vessel disease and may reflect impaired perivascular waste clearance.
- Greater short-term blood pressure (BP) variability, defined as fluctuations in BP over 24 hours, may drive ePVS development by promoting vascular dysfunction.
- While increased BP has been strongly linked to greater ePVS burden, the effect of BP variability on ePVS burden remains unclear.
- We investigated whether short-term BP variability relates to the progression of ePVS burden in older adults.

Methods & Analysis Plan

- Vanderbilt Memory and Aging Project participants free of clinical dementia and stroke (n=463, 69±9 years, 48% female) underwent 3T multimodal MRI serially over a 9-year follow-up period. See **Table 1**.
- An nnU-Net based deep learning segmentation tool, Detection Of Regions of Enlarged perivascular Spaces (DORES), was used to segment and quantify ePVS burden within the white matter and basal ganglia.
- Participants underwent 24-hour Ambulatory Blood Pressure Monitoring (ABPM) capturing systolic and diastolic BP every 30 minutes to calculate 24-hour average real variability (ARV).
- Linear mixed-effects models tested the effect of baseline short-term BP variability on the annual change in ePVS burden.
- Models were adjusted for age, sex, race/ethnicity, education, cognitive status, Framingham Stroke Risk Profile (minus age), APOE-ε4 status, intracranial volume, antihypertensive use, and mean BP, and corrected for multiple comparisons using the False Discovery Rate (FDR).

Table 1. Participant Characteristics

	Combined (n=463)	Low ARV of Systolic BP (n=155)	Middle ARV of Systolic BP (n=155)	High ARV of Systolic BP (n=153)	P-value
Age (years)	69±9	66±8	70±9	70±8	<0.001*
Follow-up duration (years)	6±3	-	-	-	-
Sex (% male)	52	43	55	59	0.13
Education (years)	16±3	16±3	16±2	16±2	0.39
Race (% non-Hispanic White)	84	85	81	86	0.52
Cognitive status at baseline (% CU)	75	73	75	76	0.82
Framingham Stroke Risk Profile (total)	10±5	9±5	11±5	12±5	<0.001*
Antihypertensive medication use (%)	47	39	47	55	0.02*
Mean systolic BP (mmHg)	136±17	129±16	137±16	141±17	<0.001*
ARV of systolic BP (mmHg)	10±2	8±1	9±1	12±1	<0.001*
Hypertension (%)	62	48	66	73	<0.001*
Diabetes (%)	16	14	13	20	0.23
Cardiovascular disease (%)	5	5	5	5	0.94

Note. Values are denoted as mean±standard deviation or frequency. Continuous variables were compared using the Kruskal-Wallis test; categorical variables were compared using the Pearson chi-squared test. Follow-up duration reflects the subset of participants with ≥2 study visits (n=287). Abbreviations: ARV, Average Real Variability; BP, Blood Pressure; CU, Cognitively Unimpaired.

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Results

- Baseline ARV of diastolic variability showed no significant association with the progression of ePVS burden in either the white matter or basal ganglia (p-values_{FDR}>0.05).
- Higher baseline ARV of systolic BP was significantly associated with a slower annual progression of white matter ePVS burden (p-values_{FDR}<0.01). See **Figure 1**.
- ARV of systolic BP was not significantly associated with the progression of basal ganglia ePVS burden. See **Figure 2**.

Figure 1. Relationship Between Baseline Systolic BP Variability and Annual Change in White Matter ePVS Burden

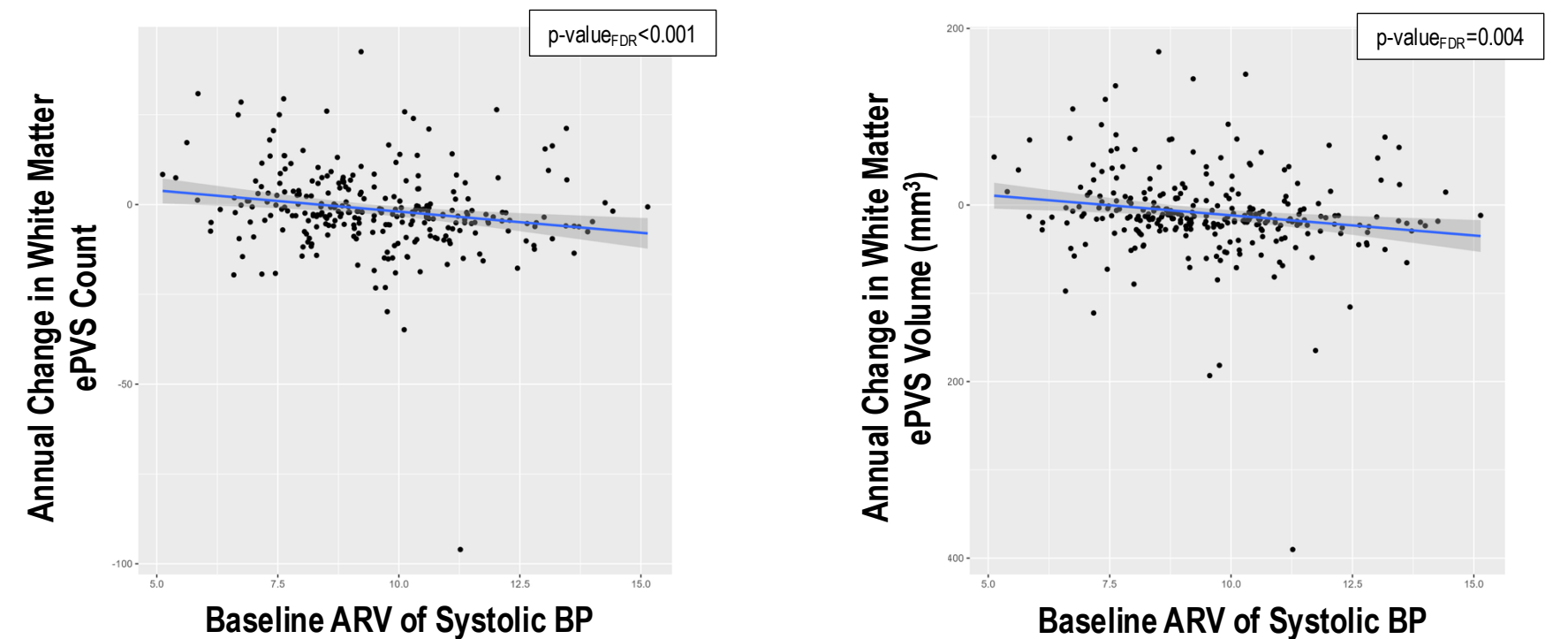
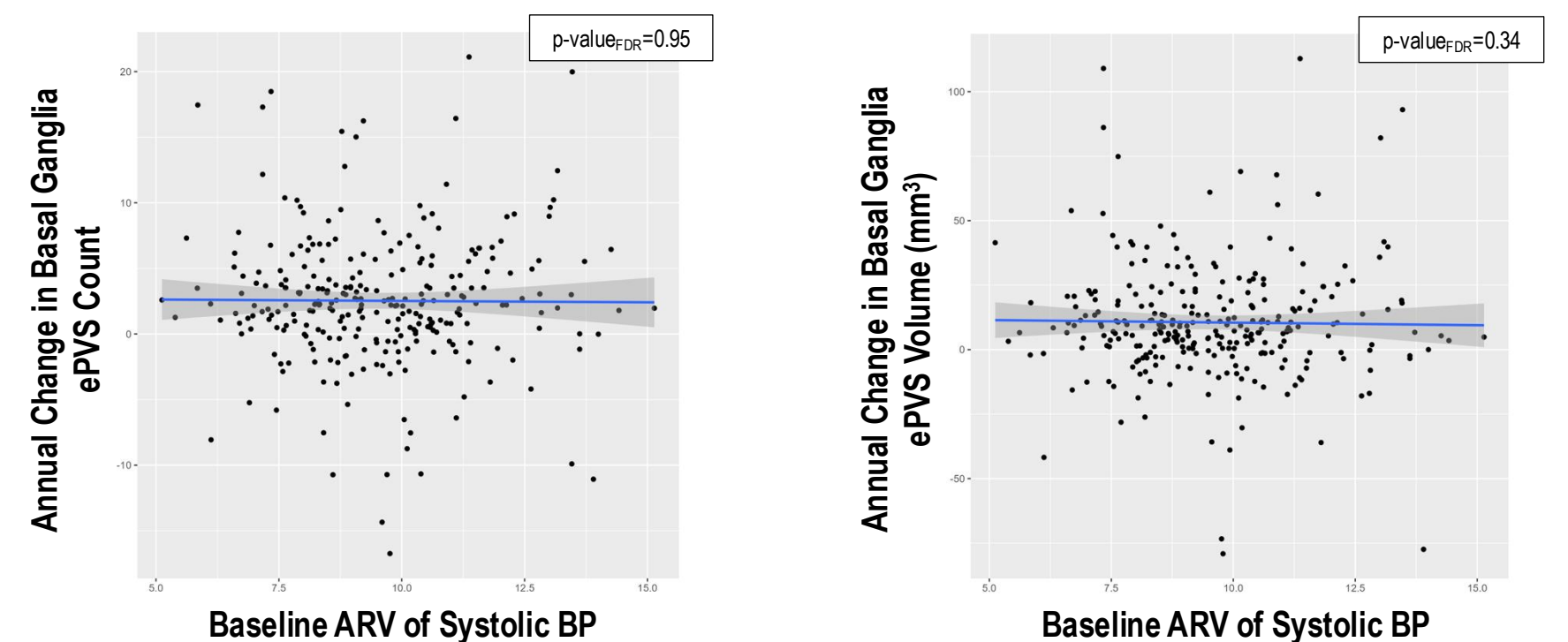


Figure 2. Relationship Between Baseline Systolic BP Variability and Annual Change in Basal Ganglia ePVS Burden



Conclusions

- Contrary to our hypothesis, greater short-term systolic BP variability was associated with slower progression of white matter ePVS burden over time.
- These paradoxical associations warrant further investigation of confounding variables and selection bias.